

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A Systematic Review of Associations between Environmental Exposures and Development of Asthma in Children Aged up to Nine Years
AUTHORS	Dick, Smita; Friend, Amanda; Dynes, Kaitlyn; Alkandari, Farah; Doust, Emma; Cowie, Hilary; Ayres, Jon; Turner, Stephen

VERSION 1 - REVIEW

REVIEWER	Erik Melén Institute of Environmental Medicine Karolinska Institutet Stockholm, Sweden
REVIEW RETURNED	26-Sep-2014

GENERAL COMMENTS	<p>This is a well-written overview paper on environmental influences on asthma in childhood, and the authors have systematically evaluated the published literature. The paper adds value to the literature, although the conclusions should be interpreted with caution given the complex associations between exposure and disease development (reverse causation etc). The study limitations have however been addressed adequately (if revised as suggested below) by the authors. I have only a few comments as outlined below:</p> <p>1) I do not agree with the abstract conclusion about antibiotics and paracetamol not being associated with asthma risk. How can this conclusion be made from the results "Four SRs were identified and these linked antenatal (135,138) and postnatal (135-137) exposure to paracetamol to the risk of asthma symptoms. There were associations between paracetamol exposure and the development of asthma OR 1.3 (139) and wheeze OR 1.2 (138)."? Same comment about antibiotics – can the authors really make the conclusion that there is no associated risk?</p> <p>2) Ref 92 refers to asthma from age 5 and above, which should be made clear in the text and table.</p> <p>3) I think it should be acknowledged as a limitation that only one paper from ongoing cohorts was included in the article. Many birth cohorts (ALSPAC, PIAMA, BAMSE, MAAS etc) have published several papers on environmental exposures at different time points and by only including the most recent paper, important data may be omitted.</p>
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REVIEWER	Stefania La Grutta
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	Institute of Biomedicine and Molecular Immunology IBIM National Research Council Italy
REVIEW RETURNED	27-Sep-2014

GENERAL COMMENTS	The paper covers a challenging field of research contributing to add more knowledge and awareness on the risk of environmental exposure on asthma in a vulnerable population.
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VERSION 1 – AUTHOR RESPONSE

Review comments on Dick et al for BMJ Open

This is a well-written overview paper on environmental influences on asthma in childhood, and the authors have systematically evaluated the published literature. The paper adds value to the literature, although the conclusions should be interpreted with caution given the complex associations between exposure and disease development (reverse causation etc). The study limitations have however been addressed adequately (if revised as suggested below) by the authors. I have only a few comments as outlined below:

1) I do not agree with the abstract conclusion about antibiotics and paracetamol not being associated with asthma risk. How can this conclusion be made from the results “Four SRs were identified and these linked antenatal (135,138) and postnatal (135-137) exposure to paracetamol to the risk of asthma symptoms. There were associations between paracetamol exposure and the development of asthma OR 1.3 (139) and wheeze OR 1.2 (138).”? Same comment about antibiotics – can the authors really make the conclusion that there is no associated risk?

WE ACCEPT THIS POINT AND HAVE AMMENDED THE ABSTRACT AND INCLUDED THE FOLLOWING NEW TEXT WHICH MORE ACCURATELY SUMMARISES THE FINDINGS. “..and although there were consistent associations between exposures to antibiotics and paracetamol in early life, these associations might reflect reverse causation. “ WE HAVE NOT AMMENDED THE DISCUSSION (PAGE 19, FIRST PAGE) WHERE WE SAID “In addition, reverse causation or confounding may explain some associations reported, e.g. postnatal exposures to antibiotics, paracetamol and perhaps pets. “

2) Ref 92 refers to asthma from age 5 and above, which should be made clear in the text and table.

WE HAVE REVISITED THIS MANUSCRIPT WHICH STATES IN THE METHODS SECTION THAT “At the age of 5 years, families of the participating children completed a questionnaire”. WE HAVE CLARIFIED IN THE TEXT AND TABLE (REF 81 IN THE TABLE) THAT CHILDREN WERE ASSESSED AT AGE 5-6 YEARS.

3) I think it should be acknowledged as a limitation that only one paper from ongoing cohorts was included in the article. Many birth cohorts (ALSPAC, PIAMA, BAMSE, MAAS etc) have published several papers on environmental exposures at different time points and by only including the most recent paper, important data may be omitted.

WE HAVE ADDED A NEW SENTENCE TO ACKNOWLEDGE THIS WELL-MADE POINT (PAGE 21).

Reviewer: 2

NO RESPONSE REQUIRED